Regulatory Education for Industry (REdI): GENERIC DRUGS FORUM

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Real-Time Communication During the CMC Review with the Office Of Pharmaceutical Quality (OPQ)

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What is Real-Time Communication?

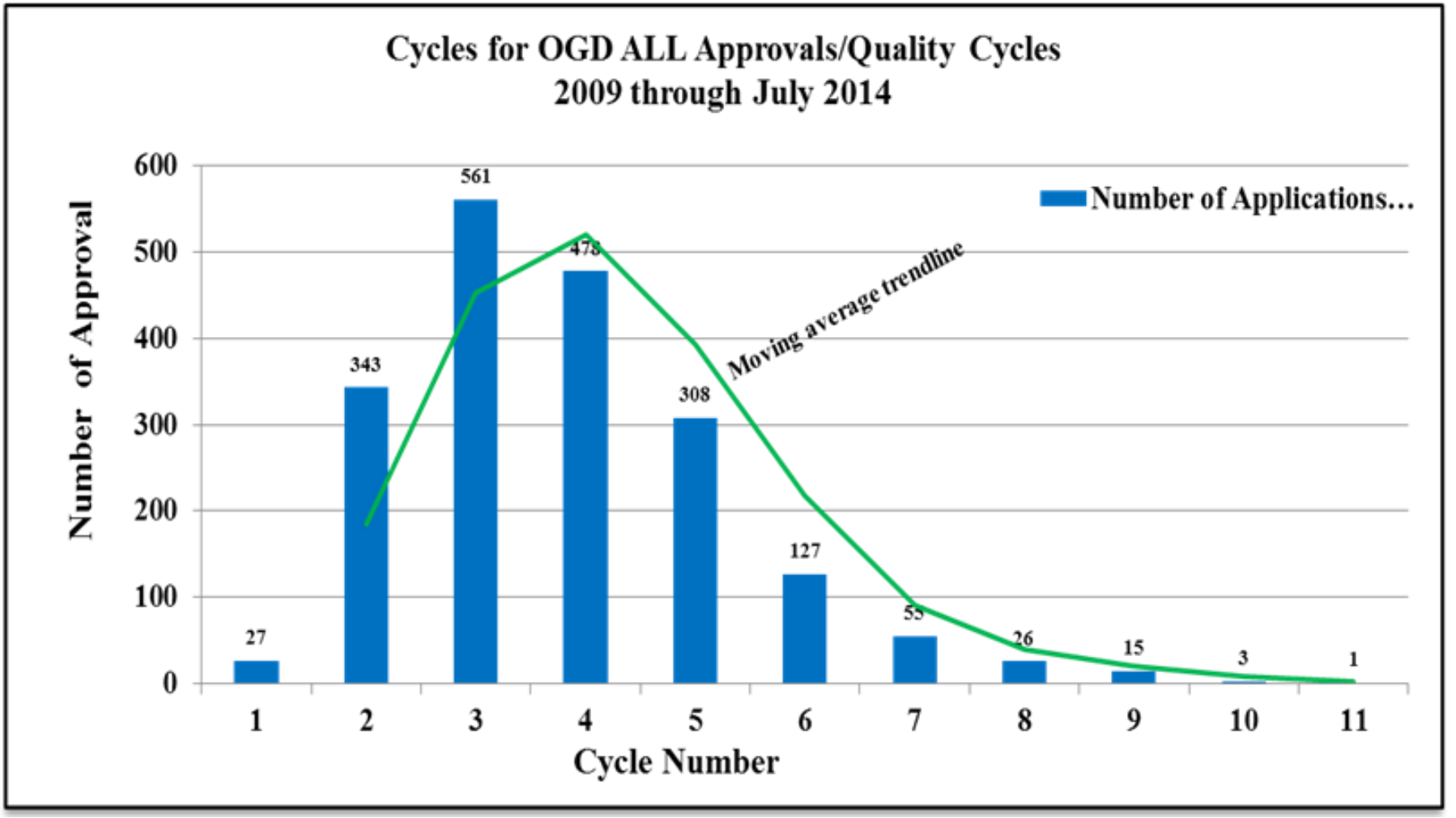
- **Real-Time Communication means communication with an ANDA applicant and an exchange of information prior to the issuance of a formal FDA action.**
  - **Action: Tentative Approval (TA), Approval (AP) and/or Complete Response (CR)**

- **Real-Time Communication does not replace OGD's formal communication methods, but rather enhances the review process in an effort to increase transparency and decrease the number of review cycles.**

Why Real-Time Communication?

- GDUFA establishes goals dates for original submissions and subsequent amendments.
- GDUFA requires open and transparent communication with the industry.
- Our current process of formal communications tends to promote multiple review cycles.
- We are striving for more informal communication to resolve issues in real-time and reduce the number of review cycles.

Number of Cycles to ANDA Approval



Advantages of Real-Time Communication

- **Transparent process and communication.**
- **Less time lost in multiple cycles.**
- **Applicant and FDA work to achieve better understanding and increased trust.**
- **Applicant can better forecast product plans.**
- **Encourages higher quality submissions.**

Definitions

- **Fatal Flaw: Significant flaws in the design of a drug product such that the proposed product will not be able to meet all conditions of use of the reference listed drug. If a fatal flaw is identified, all review activities including compliance will be stopped.**

- **Major Deficiency: A situation where necessary information does not exist in the application, or is so flawed as to require new information to be submitted. These deficiencies will require a substantial expenditure of FDA resources and must be included in a Complete Response letter from OGD. See Appendix I for examples.**

- **Minor Deficiencies: Issues that cannot be resolved using the real time communication process, and must be included in a Complete Response letter from OGD.**

- **Chemistry Information Request(s) and Clarification Question(s): Issues which could be resolved during the real time communication process.**

Definitions

- **Regulatory Business Project Manager (RBPM): A centralized project manager for the quality assessment of applications. RBPMs are the former PQRPMs with expanded leadership role.**

- **OGD Target Action Date (TAD): An internal deadline for formal FDA action on a submission. TADs are assigned by OGD after consultation with the review disciplines, including OPQ. A TAD is not a GDUFA goal date and will generally be earlier in time than the applicable GDUFA goal date.**

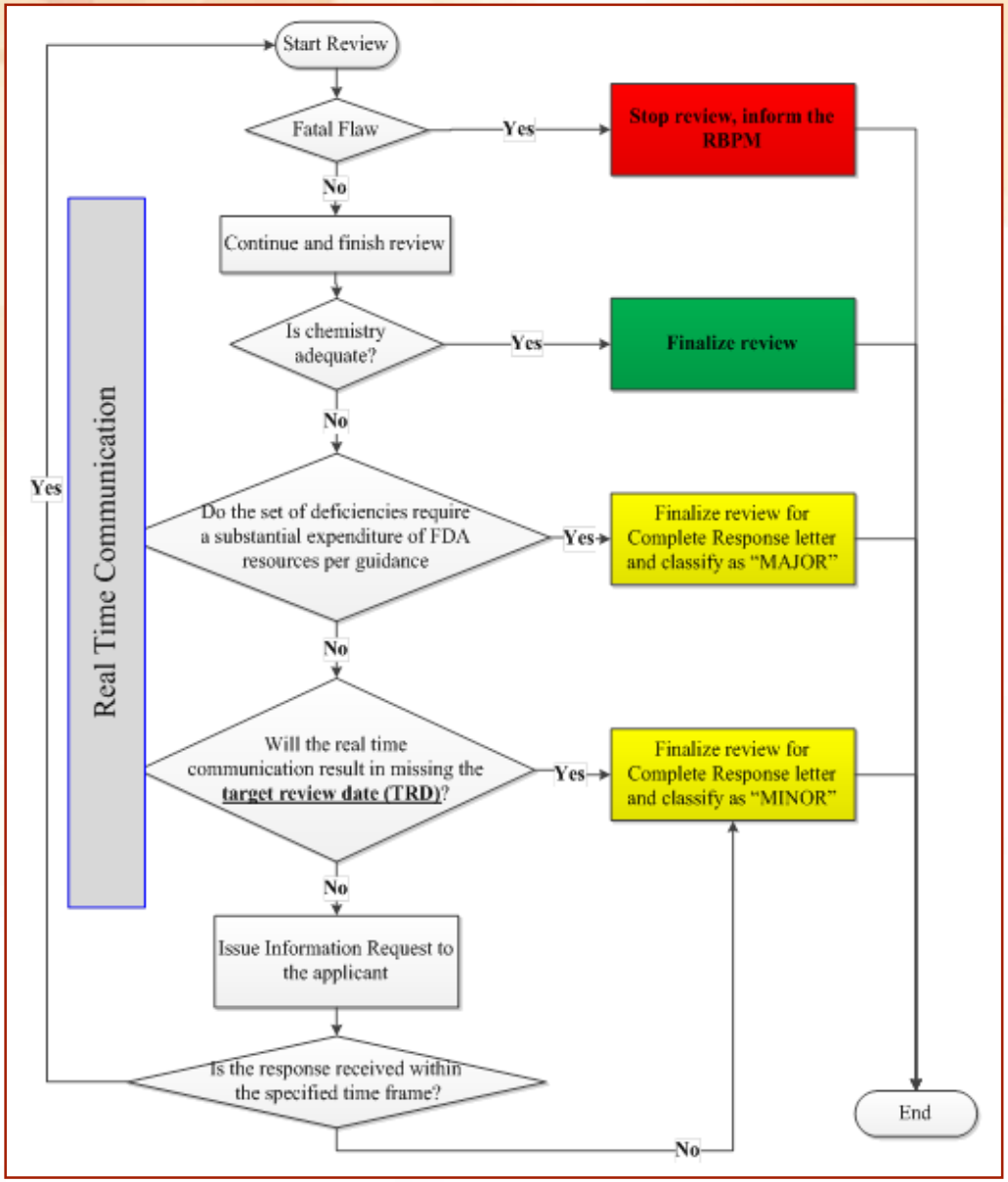
- **Discipline Review Date (DRD): A deadline established at which time the results of a discipline (e.g. chemistry) review process must be communicated by the Office of Pharmaceutical Quality (OPQ) to the Office of Generic Drugs (OGD). This date is established to ensure all commitments required under GDUFA are met.**

- **Target Review Date (TRD): A deadline set according to OPQ management policy by which a chemistry review must be completed. This date is established to ensure that the RBPM has sufficient time to complete all tasks prior to communicating the results of the review to OGD.**

Real-Time Communication Process

- **The Real-Time Communication process requires:**
  - **Understanding and following the Flow Chart in the next slide, and**
  - **Always meeting all Target Review Dates and Discipline Review Dates.**

Real-Time Communication Process



Points to Consider

1. **A response to all items in an Information Request is preferable, and the applicant is encouraged to provide a complete response to all the requests. However, if the applicant cannot provide a full response to all items, they should provide a response to as much as they can, with the realization that the remaining items will have to be addressed in the future, either as an additional information request or as part of a Action Letter issued by OGD.**

Points to Consider

2. **The normal maximum response time for the applicant is 30 calendar days and extensions of the response times are discouraged. However, the response time can be extended a short period of time (e.g. 1 or 2 days) if all the requested information can be addressed with this extension. We encourage industry to communicate with the OPQ RBPM to request the 1 to 2 day extension and also to notify the RBPM if the requested IR request response date will not be met.**

Note: Discipline Review Dates and GDUFA goals must be met in all circumstances.

Points to Consider

3. **The reviewer may make a telephone call to the applicant after reviewing a response if that call will quickly resolve any remaining issues. However, a RBPM should always be present and care must be taken to meet Discipline Review Dates and GDUFA goals. The reviewer should work with the RBPMs to make sure any telephone requests are adequately documented.**

Points to Consider

4. **If the applicant does not respond or contact the RBPM, Real Time Communication is ended at the end of the allotted time and the Information Requests become Minor Deficiencies to be included in a Complete Response Letter from OGD.**

Points to Consider

5. **It should be made clear at the start of the Real Time Communication process that unsolicited information in a response is not acceptable, and may be considered a Major Amendment for original applications submitted before October 1, 2014, and a Tier 2 Unsolicited Amendment for original applications submitted after October 1, 2014.**

Appendix I

- **For examples of what could be considered Major Deficiencies, please read "*Guidance for Industry ANDA Submissions - Amendments and Easily Correctable Deficiencies Under GDUFA*." Additional examples may include lack of risk mitigation for high-risk Critical Quality Attributes (CQAs) or manufacturing processes, missing pivotal batch data, insufficient data to demonstrate drug substance sameness (especially for complex drug products), insufficient information to support Q3 attribute sameness for the purpose of biowaiver, fundamental formulation flaws that necessitate reformulation, and absence of analytical methods or method validation.**

http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM404440.pdf

Real-Time Communication

Questions?

Evaluation: surveymonkey.com/s/GDF-D2S6